IN THE CLAIMS

Claims 10, 11 and 22-27 have been previously canceled, while claims 1-9, 17-21, 28-31, and 37-46 are presently under consideration in this application (with their respective status shown parenthetically). Claims 12-13, 15-16 and 32-36 have been withdrawn from consideration, while claim 14 had been previously withdrawn from consideration.

1. (Previously Presented) A method of selection and/or identifying one or more protein affinity ligands, wherein the affinity ligands are antibodies, that bind to one or more proteins of interest, comprising the steps of:

(A) obtaining a real or theoretical mass spectrometry based characterization of the one or more proteins by either:

i. Subjecting the one or more proteins to a mass spectrometry based characterization; or

ii. Predicting the mass spectrometry based characterization from known data;

(B) utilizing the one or more proteins either individually or as a mixture to:

i. Generate one or more antibodies thereto by immunization; and/or

ii. Select, using a single or multiple rounds of binding, one or more antibodies thereto;

(C) screening to one or more antibodies generated in step B(i) and/or multiple antibodies selected by step (B)(ii) by:

i. adding a mixture of proteins or the one or more proteins individually to the one or more antibodies generated in step (B)(i) or the one or more antibodies selected in step (B)(ii), each antibody being used individually, and

ii. after removing any proteins which have not bound, eluting the at least one protein has bound;

(D) subjecting the at least one eluted protein to mass spectrometry based characterization; and

(E) by comparing the mass spectrometry based characterization obtains in steps (A) and (D), selecting and/or identifying that at least one antibody that binds to the one or more proteins of interest.

2. (Previously Presented) A method as claimed in claim 1 wherein the one or more proteins of interest have been previously resolved by 2D electrophoresis.

3. (Original) A method as claimed in claims 1 or 2 wherein between steps (B) and (C) the antibodies obtained in step (B)(i.) are cloned.

4. (Previously Presented) A method as claimed in claim 1 wherein the one or more proteins of interest are present in a mixture of proteins.

5. (Previously Presented) A method as claimed in claim 1 wherein the method is a method for selecting and identifying protein affinity ligands to a plurality of proteins.

6. (Previously Presented) A method as claimed in claim 1 wherein the other mass spectrometry based characterization includes acquisition of sequence tag data.

7. (Previously Presented) A method as claimed in claim 1 wherein the antibodies optionally generated in step (B)(i) are immobilized on a support comprising nitrocellulose or PVDF.

8. (Previously Presented) A method as claimed in claim 7 wherein the support upon which the antibodies are immobilised and the nitrocellulose or PVDF are treated with an oligosaccharide or polyvinylpyrrolidine solution to block any remaining binding sites.

9. (Original) A method as claimed in claim 8 wherein the oligosaccharide is ficoll.

10-11. (Canceled)

12. (Withdrawn) A method generating monoclonal antibodies to one or more targeted proteins comprising the steps of:

(a) resolving a complex protein mixture;

(b) subjecting the resolved protein(s) to peptide mass fingerprinting to obtain a peptide mass profile or obtain a theoretical peptide mass profile;

(c) utilizing one or more of the resolved proteins to generate one or more monoclonal antibodies thereto;

(d) adding the or another complex protein mixture to the one or more monoclonal antibodies generated in Step (c), to select those proteins which bind the one or more monoclonal antibodies, and subjecting the selected proteins(s) to peptide mass fingerprinting to obtain a peptide mass profile;

(e) comparing the peptide mass profiles obtained in steps (b) and (d); and

(f) selecting one or more monoclonal antibodies of interest.

13. (Withdrawn) A method of generating an antibody library comprising the steps of:

(a) resolving a complex protein mixture and subjecting the resolved protein(s) to peptide mass finger printing to obtain a peptide mass profile; or

(b) obtaining a theoretical peptide mass profile for a protein which is sought;

(c) utilizing the or the other complex protein mixture to generate one or more monoclonal antibodies thereto;

(d) adding the one or the other complex protein mixture to the one or more monoclonal antibodies generated in Step (c) to select those proteins which bind the one or more monoclonal antibodies, and subjecting the selected protein(s) to peptide mass fingerprinting to obtain a peptide mass profile;

(e) comparing the peptide mass profiles obtained in steps (a or b) and (d); and

(f) identifying the monoclonal antibodies of interest.

14. (Withdrawn) A process for selecting desired members of an affinity ligand library comprising the steps of:

(a) resolving a complex protein mixture and subjecting the resolved protein(s) to peptide mass finger printing to obtain a peptide mass profile; or

(b) obtaining a theoretical peptide mass profile for a protein which is sought;

(c) utilizing one or more of the resolved proteins to select one or more affinity ligands from a library;

(d) adding the or another complex protein mixture to the one or more affinity ligands generated in step (c) to select those proteins which bind the one or more affinity ligands, and subjecting the selected protein(s) to peptide mass fingerprinting to obtain a peptide mass profile;

(e) comparing the peptide mass profiles obtained in steps (a or b) and (d); and

(f) selecting one or more affinity ligands of interest

15. (Withdrawn) A method of screening an antibody to a protein characterized in that the antibody is generated or selected using an impure protein or a complex protein mixture and then identified by comparing a mass spectrometry based characterization obtained from the protein/proteins for which it is specific with that of a mass spectrometry based characterization which is theoretical for said protein/proteins or is obtained from the impure protein or complex protein mixture.

16. (Withdrawn) A method of selecting an antibody specific to a given peptide characterized in that the antibody is selected by comparing a mass spectrometry based characterization of the protein/proteins released from the antibody to which it binds with a mass spectrometry based characterization which is theoretical for said protein/proteins or is obtained from the known protein.

17. (Previously Presented) A method as claimed in claims 1, 2, 7, 8, or 9-wherein the mass spectrometry based characterization is obtained by mass spectrometry.

18. (Previously Presented) A method as claimed in claims 1, 2, 7, 8, or 9-further comprising the use of automated well plate handling technology and automated high-throughput mass spectrometry.

19. (Previously Presented) A method as claimed in claim 2 wherein the antibodies generated in step (B)(i.) are immobilized on a support comprising nitrocellulose or PVDF.

20. (Previously Presented) A method as claimed in claim 19 wherein the support upon which the antibodies are immobilized are treated with an oligosaccharide or polyvinylpyrrolidine solution to block any remaining binding sites.

21. (Previously Presented) A method as claimed in claim 20 wherein the oligosaccharide is ficoll.

22-27. (Canceled)

28. (Previously Presented) A method as claimed in claim 2 wherein the one of more proteins of interest are present in a mixture of proteins.

29. (Previously Presented) A method as claimed in claim 2 wherein the method is method for selecting and identifying protein affinity ligands to a plurality of proteins.

30. (Previously Presented) A method as claimed in claim 2 wherein the other mass spectrometry based characterization includes acquisition of sequence tag data.

31. (Previously Presented) The method of claim 1 wherein said mass spectrometry based characterization is a peptide mass fingerprint.

32. (Withdrawn) The method of claim 15 wherein said mass spectrometry based characterization is a peptide mass fingerprint.

33. (Withdrawn) The method of claim 16 wherein said mass spectrometry based characterization is a peptide mass fingerprint.

34. (Withdrawn) A method of selecting and/or identifying at least one antibody which binds at least one protein of interest, comprising the steps of:

(A) obtaining a theoretical mass spectrometry-based characterization of a target protein;

(B) providing an antibody which selectively binds to said target protein;

(C) isolating and collecting said target protein through affinity binding with said antibody;

(D) analyzing said collected target protein for said pre-selected mass spectrometry-based characterization; and

(E) comparing the mass spectrometry-based characterization obtained in step (D) with the theoretical mass spectrometry-based characterization of step (A).

35. (Withdrawn) The method of selecting and/or identifying at least one antibody which binds at least one protein of interest recited in claim 34 wherein said mass spectrometry-based characterization is a peptide mass fingerprint.

36. (Withdrawn) The method claim 35, further comprising the step of obtaining an additional mass spectrometry-based characterization in addition to said peptide mass fingerprint.

37. (Previously Presented) A method as claimed in claim 1 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

38. (Previously Presented) A method as claimed in claim 37 wherein the eluting agent is formic acid.

39. (Previously Presented) A method as claimed in claim 8 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

40. (Previously Presented) A method as claimed in claim 39 wherein the eluting agent is formic acid.

41. (Previously Presented) A method as claimed in claim 19 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

42. (Previously Presented) A method as claimed in claim 41 wherein the eluting agent is formic acid.

43. (Previously Presented) A method as claimed in claim 20 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

44. (Previously Presented) A method as claimed in claim 43 wherein the eluting agent is formic acid.

45. (Previously Presented) A method as claimed in claim 21 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

46. (Previously Presented) A method as claimed in claim 45 wherein the eluting agent is formic acid.

CONCLUSION

Applicant submits that this paper, including the text of all pending claims according to Revised Amendment Practice under 37 C.F.R. § 1.121, constitutes a complete response to the Office Action mailed July 21, 2004, and when taken with the Election filed with the Office on April 28, 2004, constitutes a complete response to the Office Action mailed November 3, 2003.

Respectfully submitted,

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By: _____

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